

Figure 1

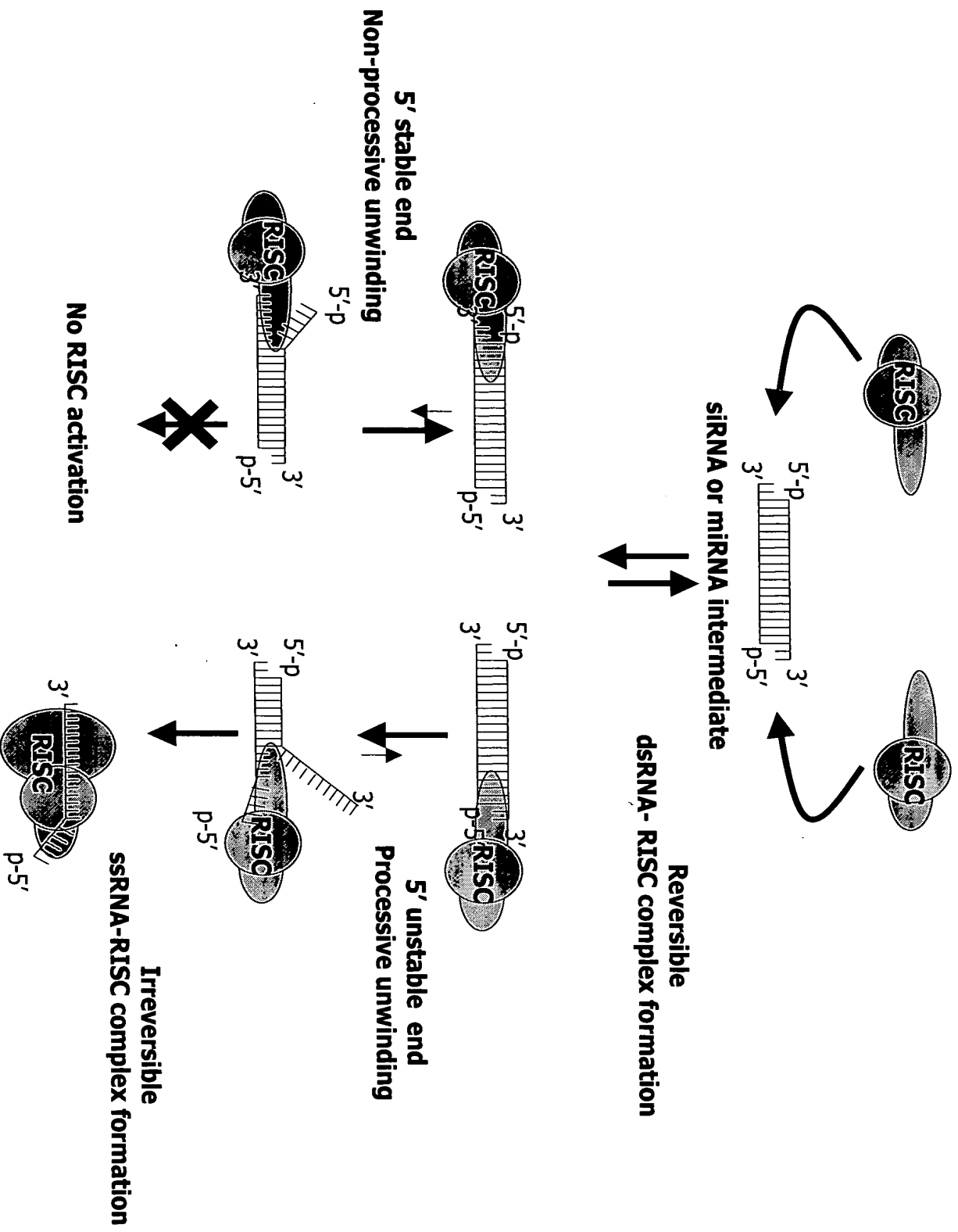


Figure 2

**siRNA panel (270)**

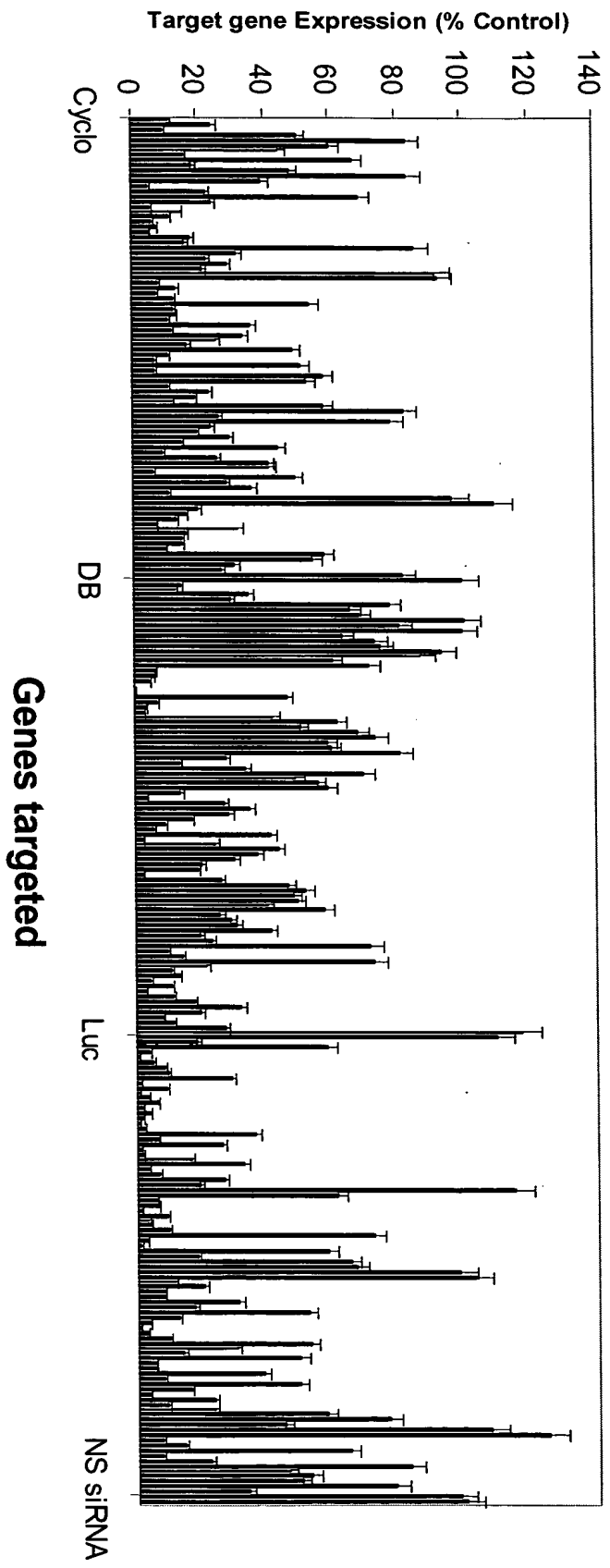


Figure 3a

**siRNA functionality is independent from the cell line**

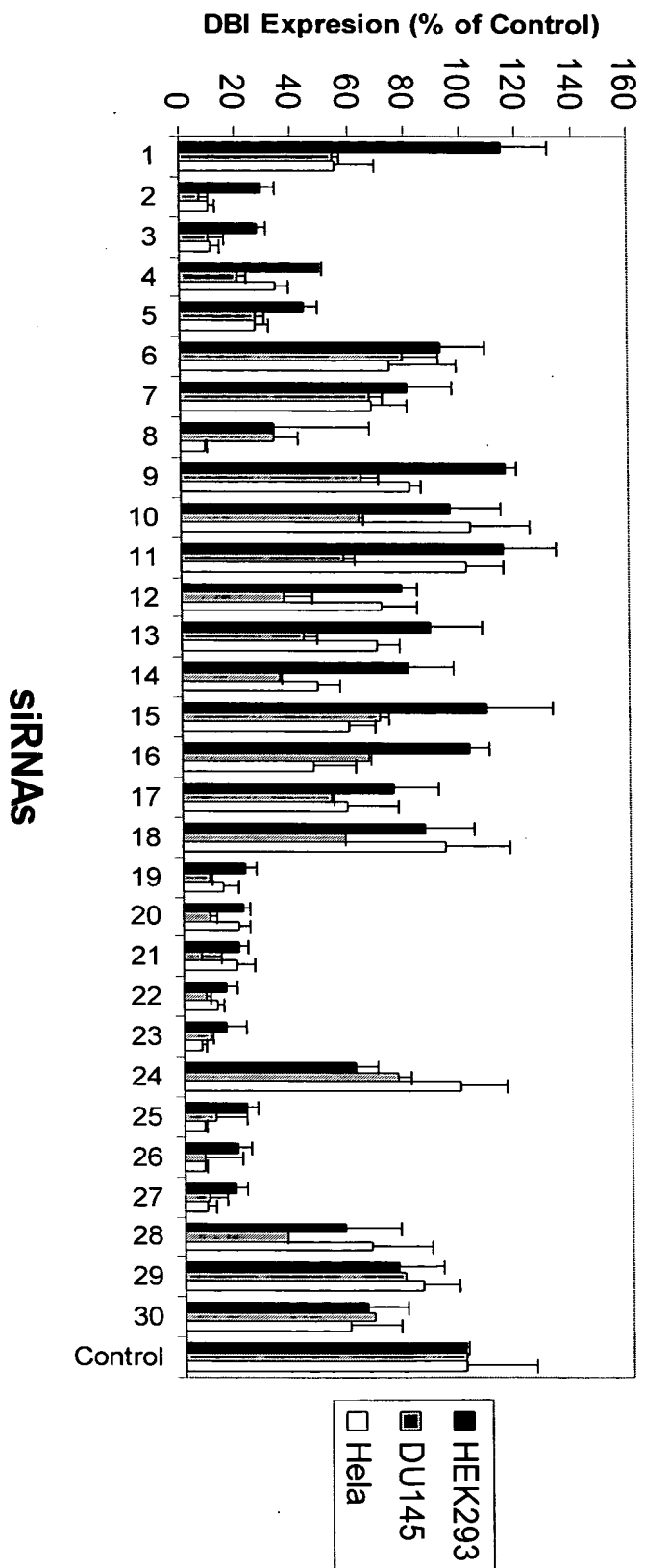


Figure 3b

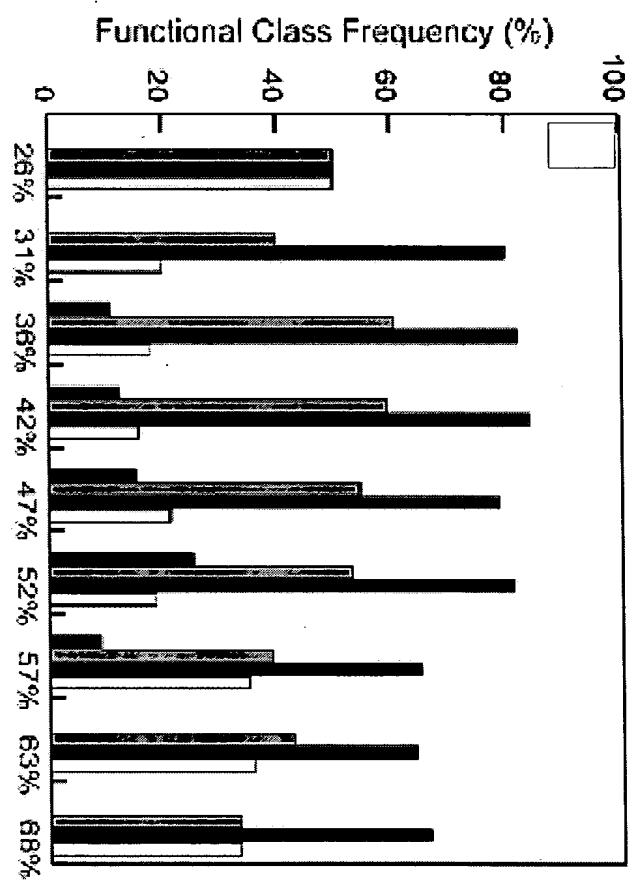


Figure 3c

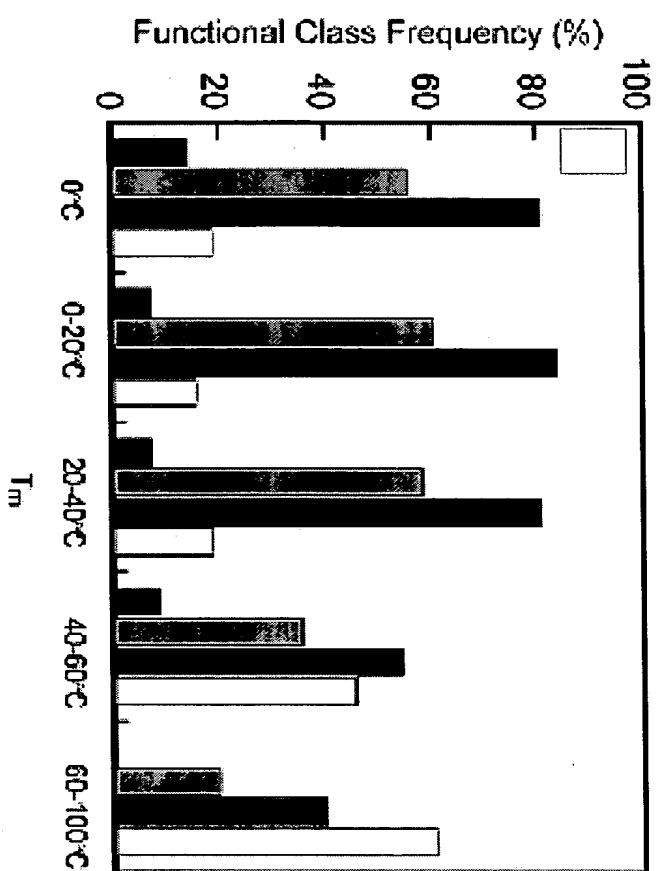


Figure 4

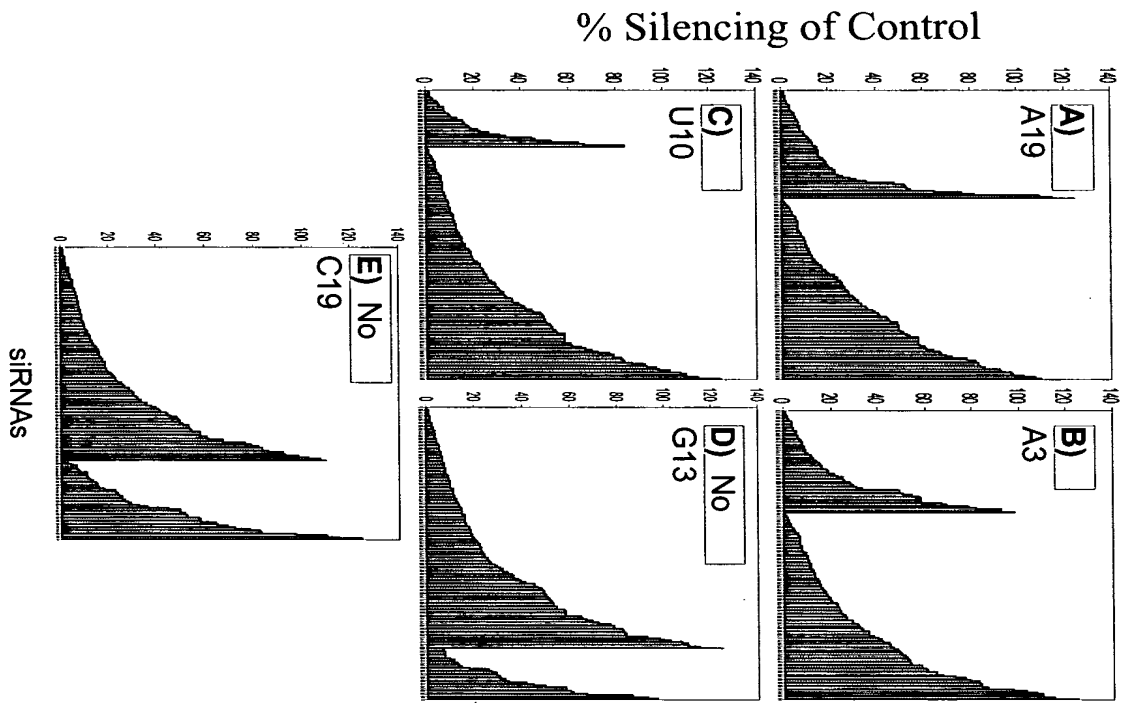


Figure 5A

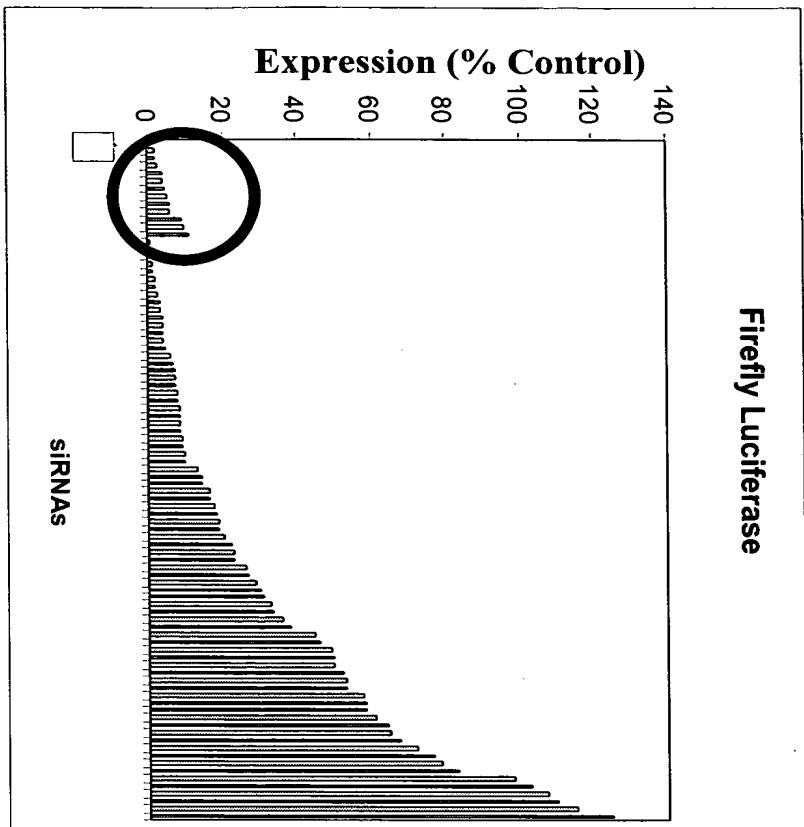


Figure 5B

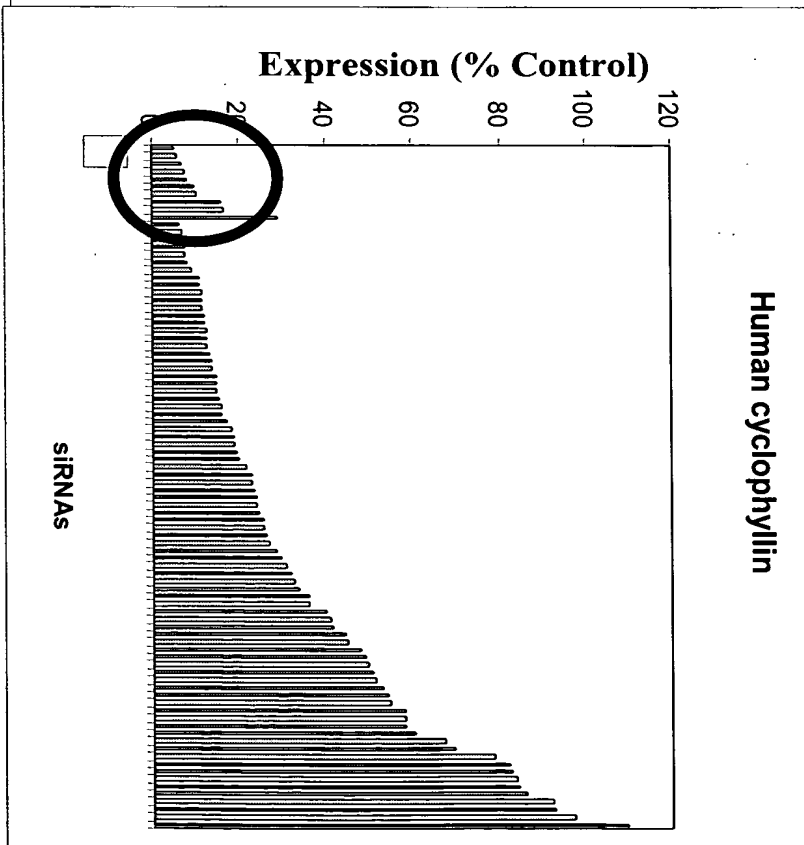


Figure 6a

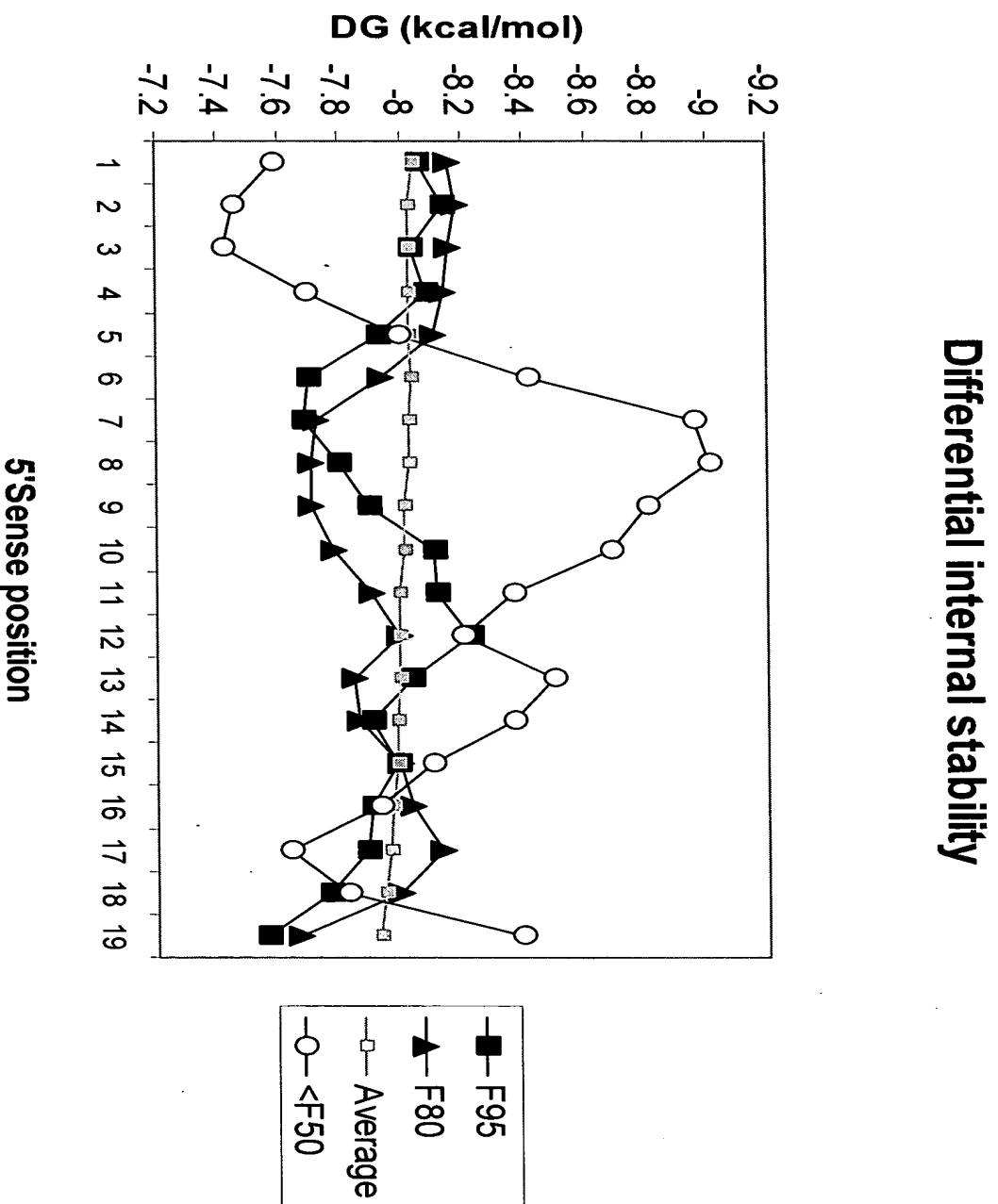


Figure 6b

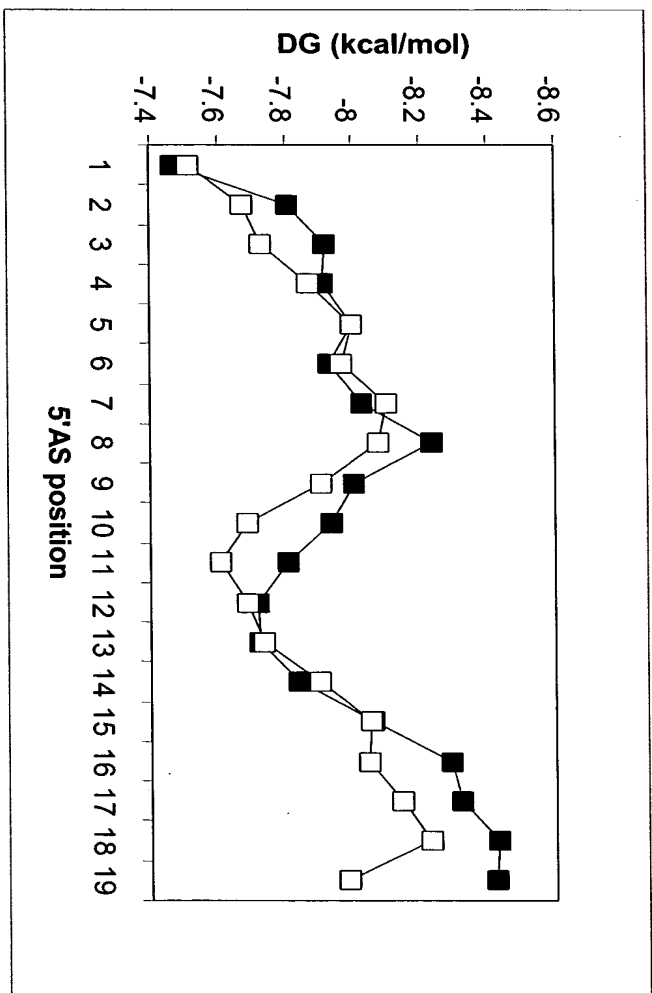
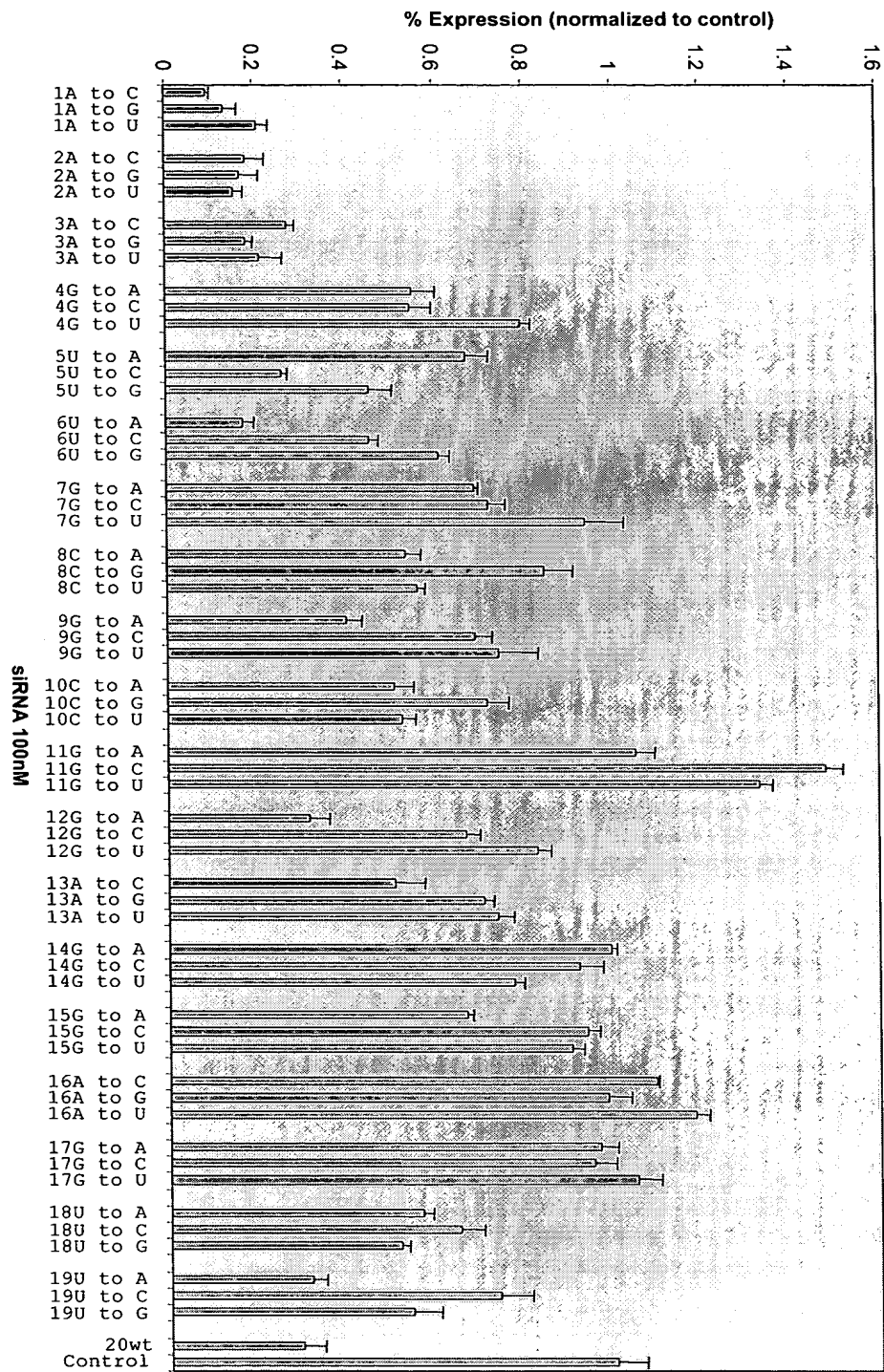
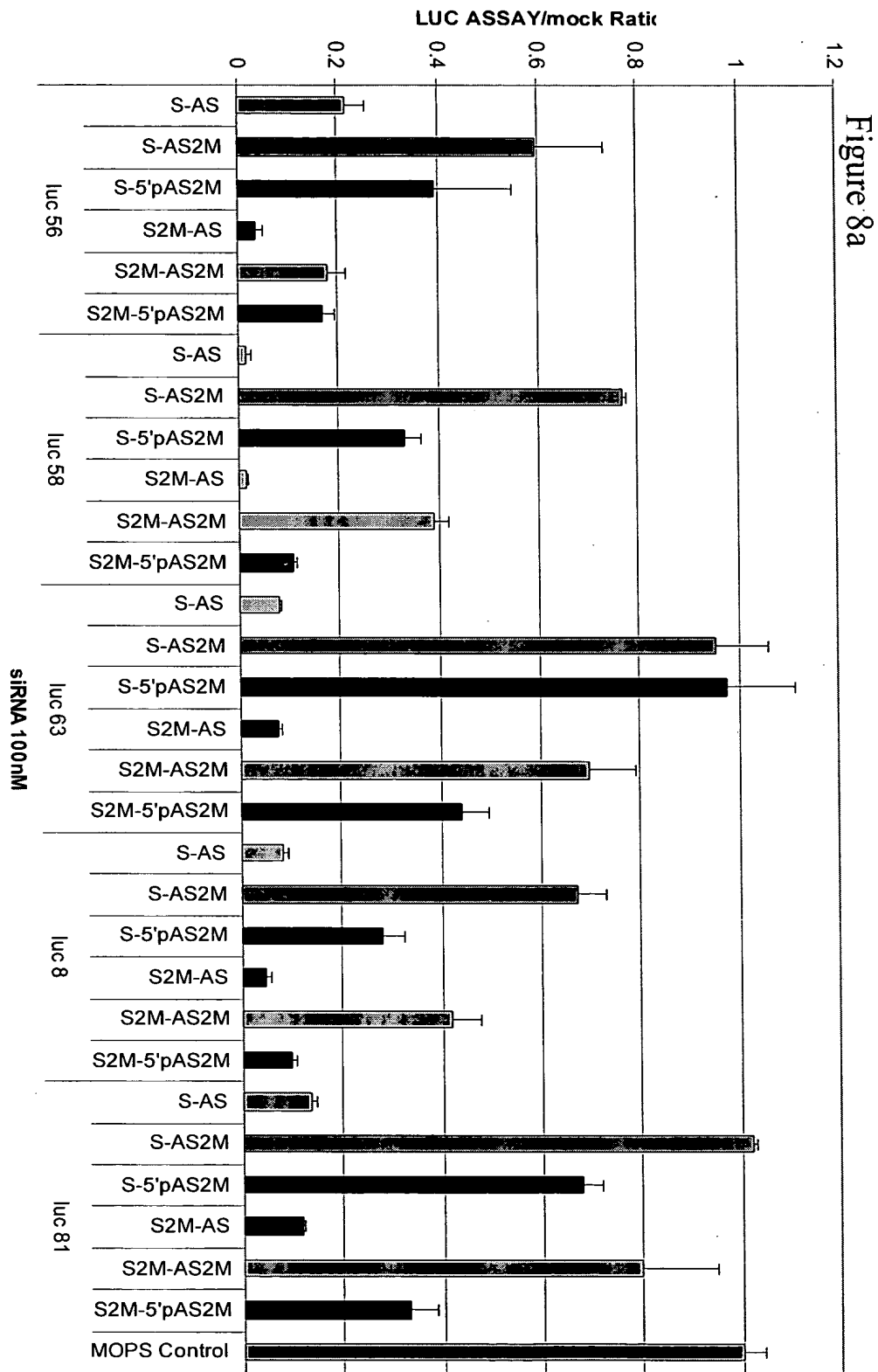




Figure 7



TARGET Screen Normalized LUC ASSAY 293 cells



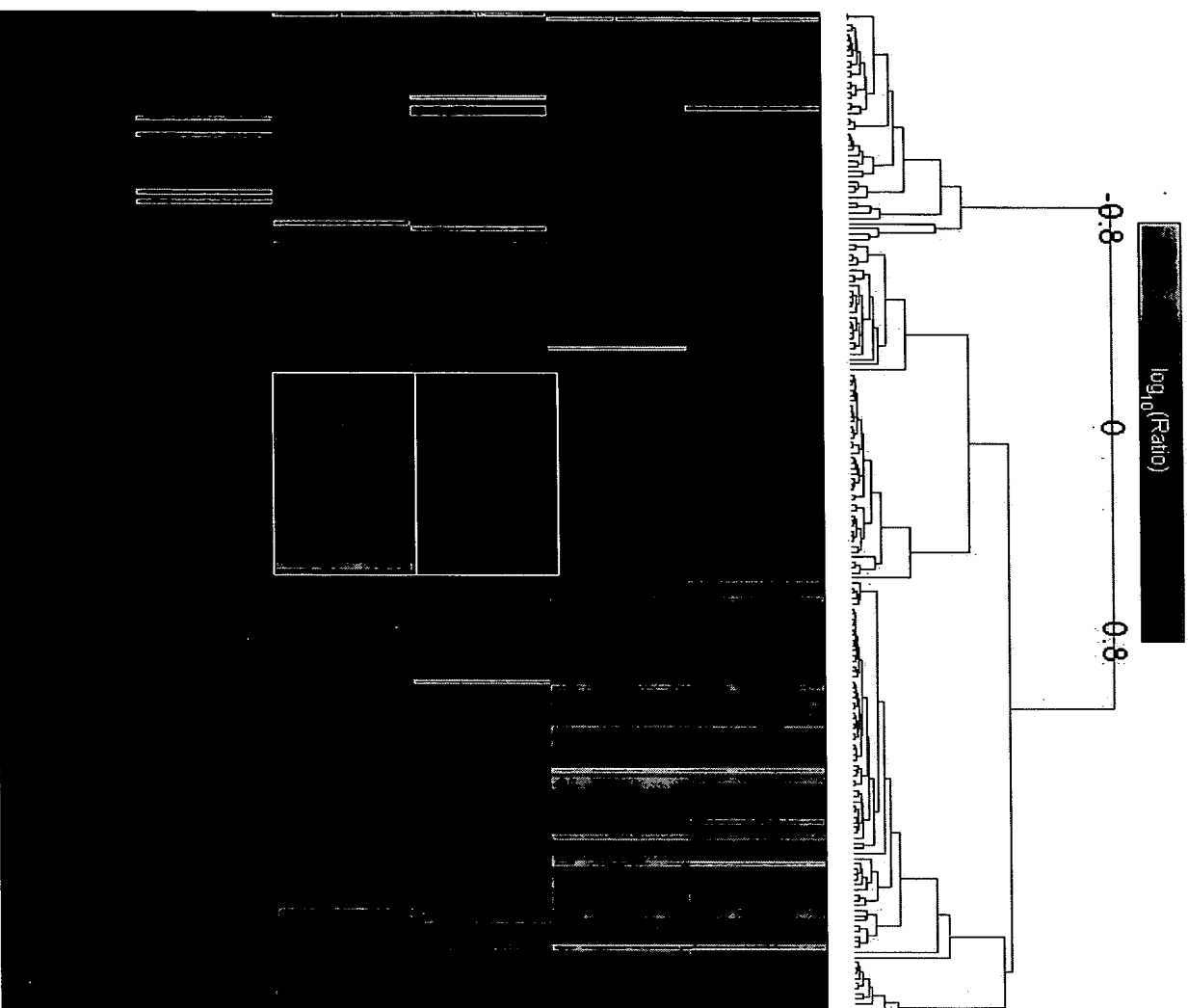


Figure 8b

IGF1R-3

Sense strand modified

IGF1R-3

CLUSTER ANALYSIS SUMMARY:  
 15 Aug 2003 17:53:57  
 15 from IGF1R-3 public Scheller RNAiDharmacon2003 juvIGF1R chem mod1 mat  
 Clustering Parameters: algorithm = gene, similarity measure = correlation-based, metric type =, link  
 Statistics: 193 genes in 6 experiments selected from 25061 genes in 6 experiments

Figure 9

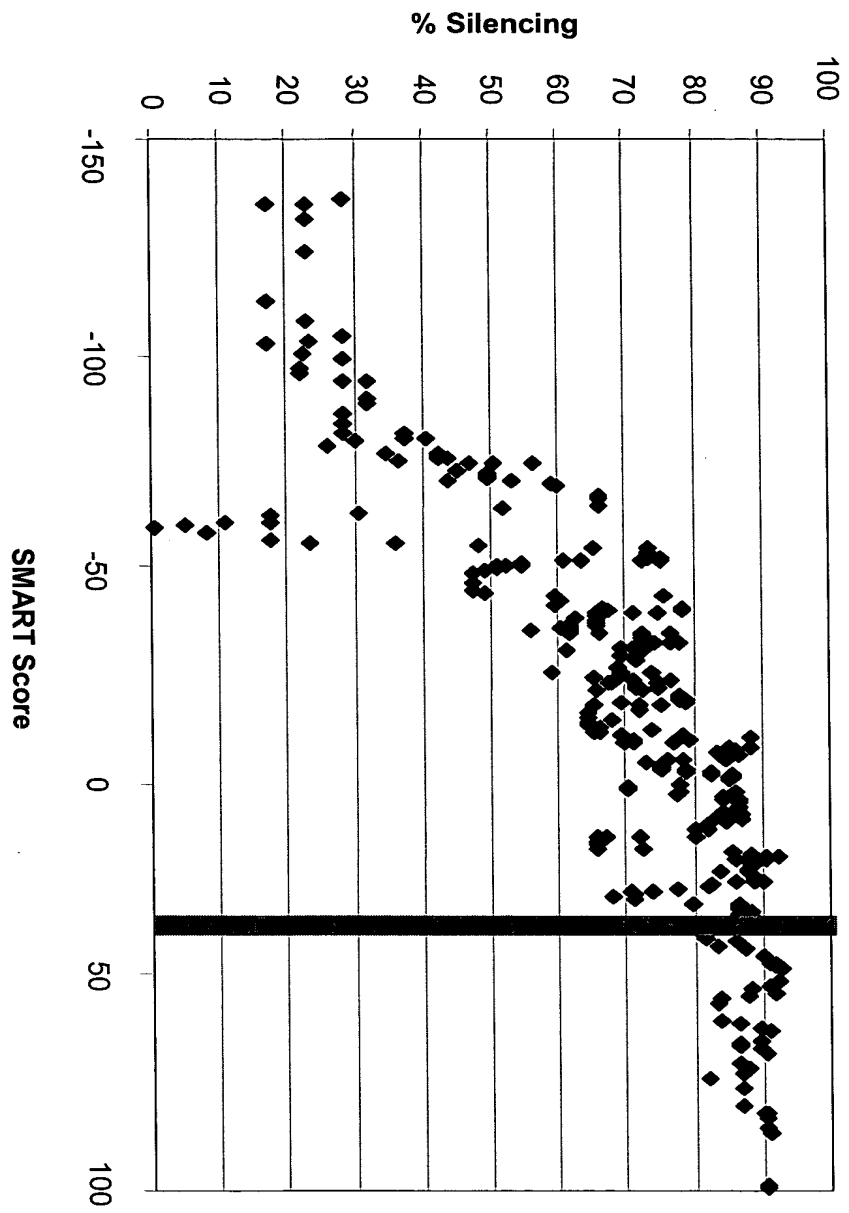


Figure 10a-f

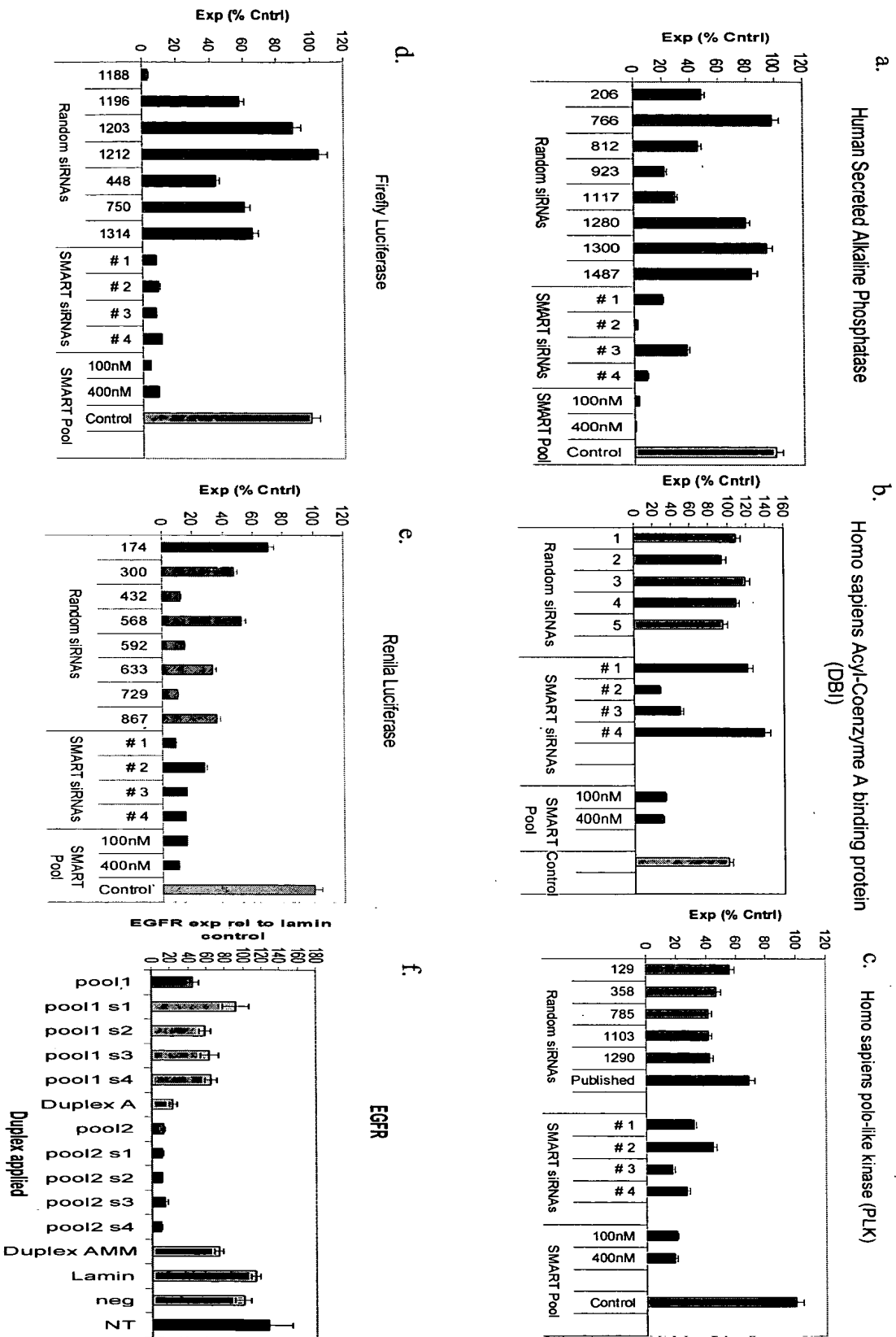


Figure 11

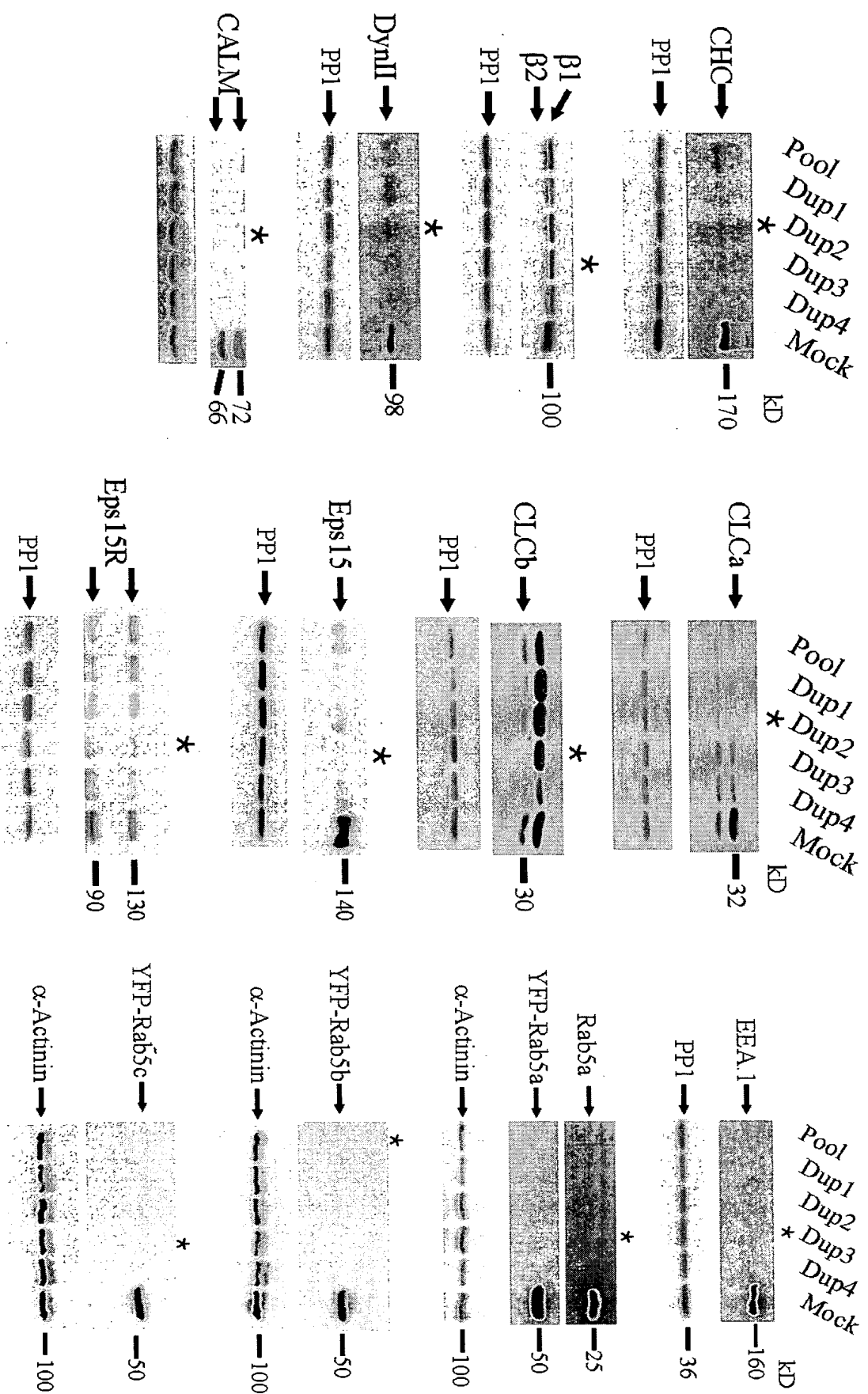


Figure 12

# Rational selection validation

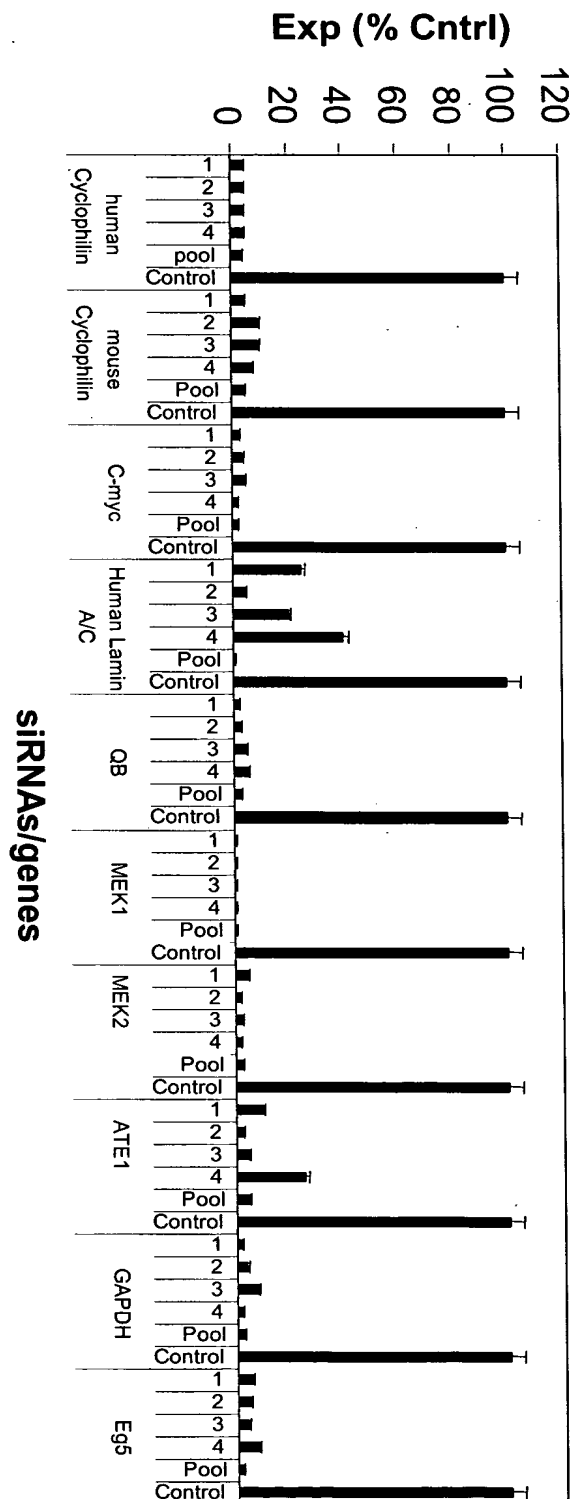


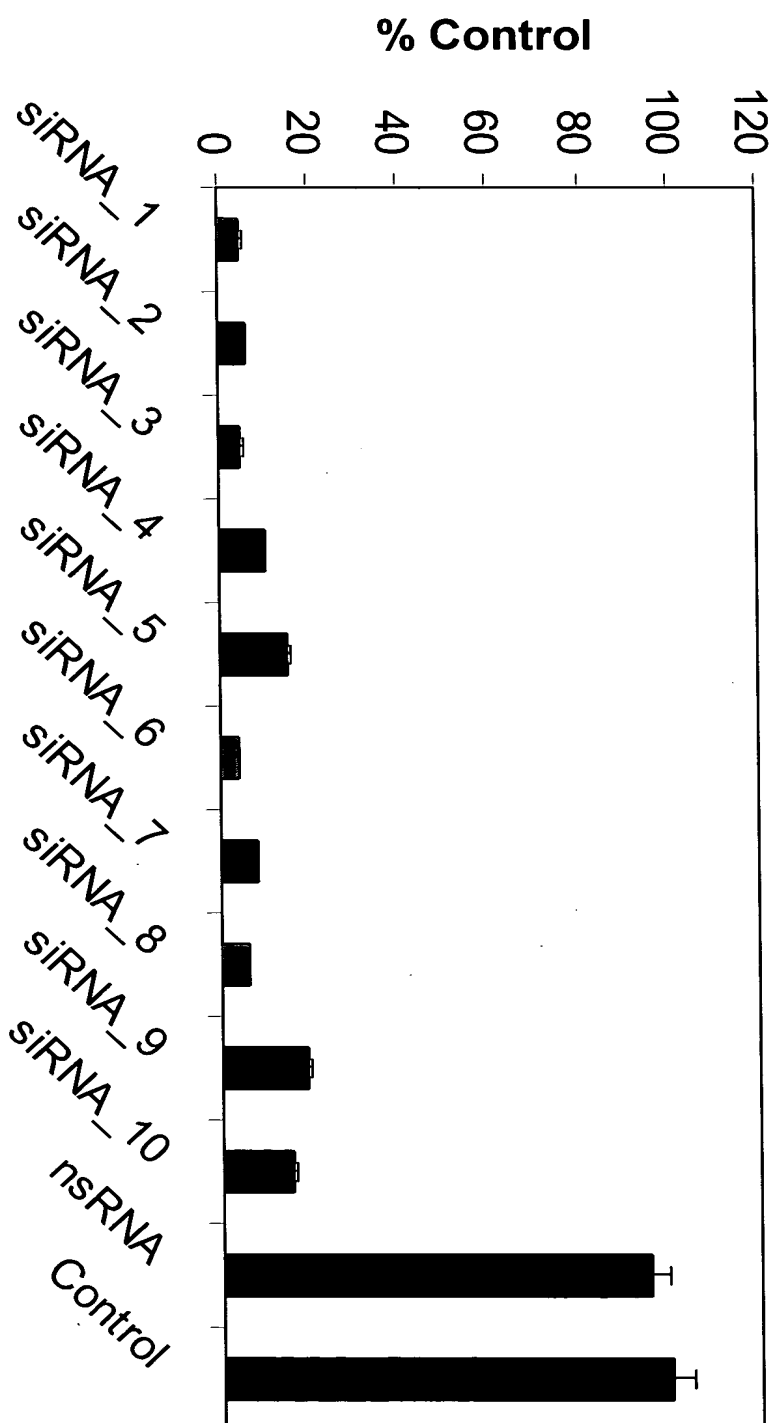
Figure 13 Sequences of top Bcl2

sirRNA 1 GGGAGAUAGUGAUGAAGUA  
sirRNA 2 GAAGUACAUCCAUUAUAAG  
sirRNA 3 GUACGACAACCGGAGAUUA  
sirRNA 4 AGAUAGUGAUGAAGUACAU  
sirRNA 5 UGAAGACUCUGCUCAGUUU  
sirRNA 6 GCAUGCGGCCUCUGUUUGA  
sirRNA 7 UGCGGCCUCUGUUUGAUUU  
sirRNA 8 GAGAUAGUGAUGAAGUACA  
sirRNA 9 GGAGAUAGUGAUGAAGUAC  
sirRNA 10 GAAGACUCUGCUCAGUUUG



Figure 14

**Bcl-2 knockdown by 10 rationally designed siRNAs at  
100 nM concentration**



# Reporter gene individual siRNAs walk

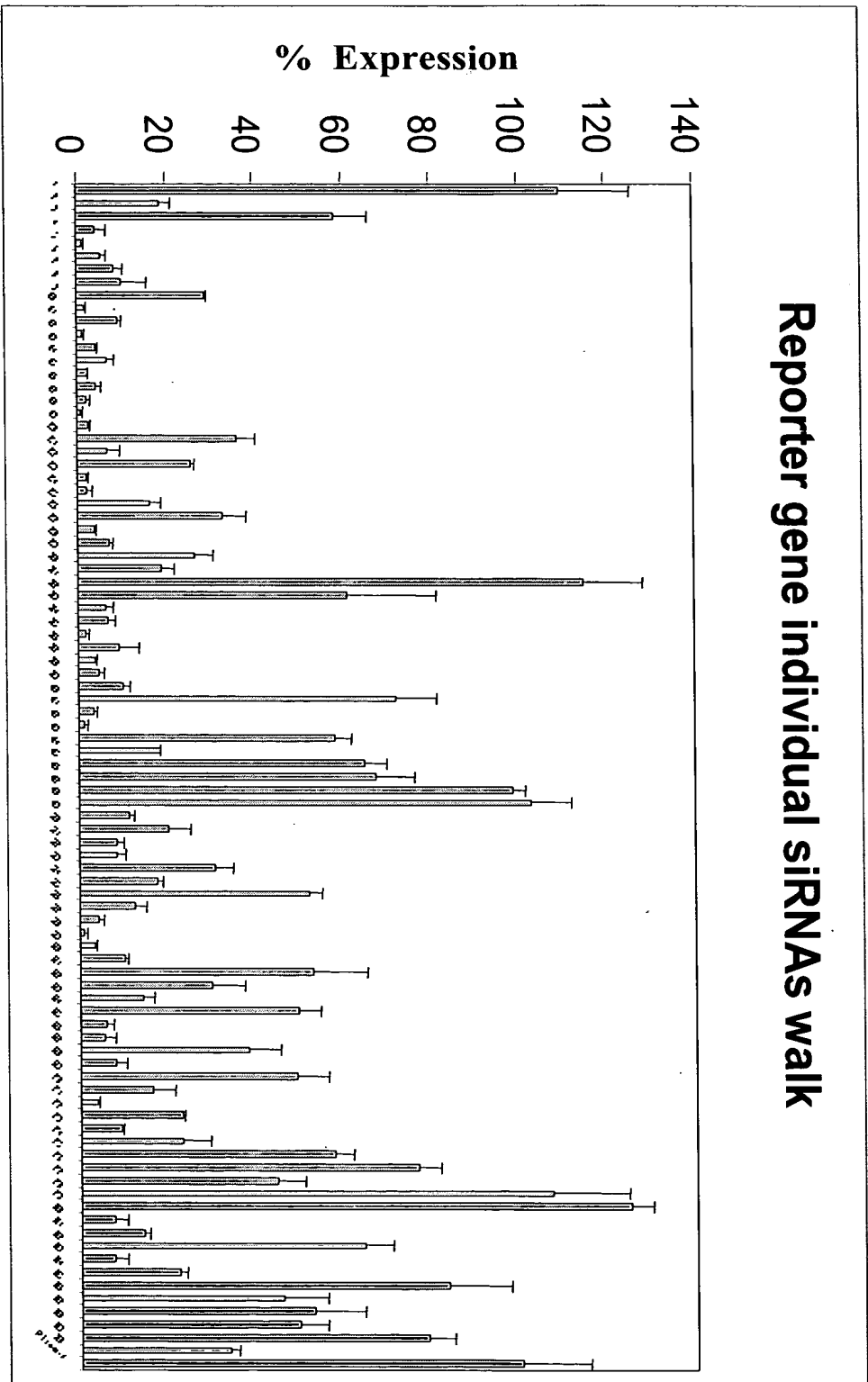


Figure 15

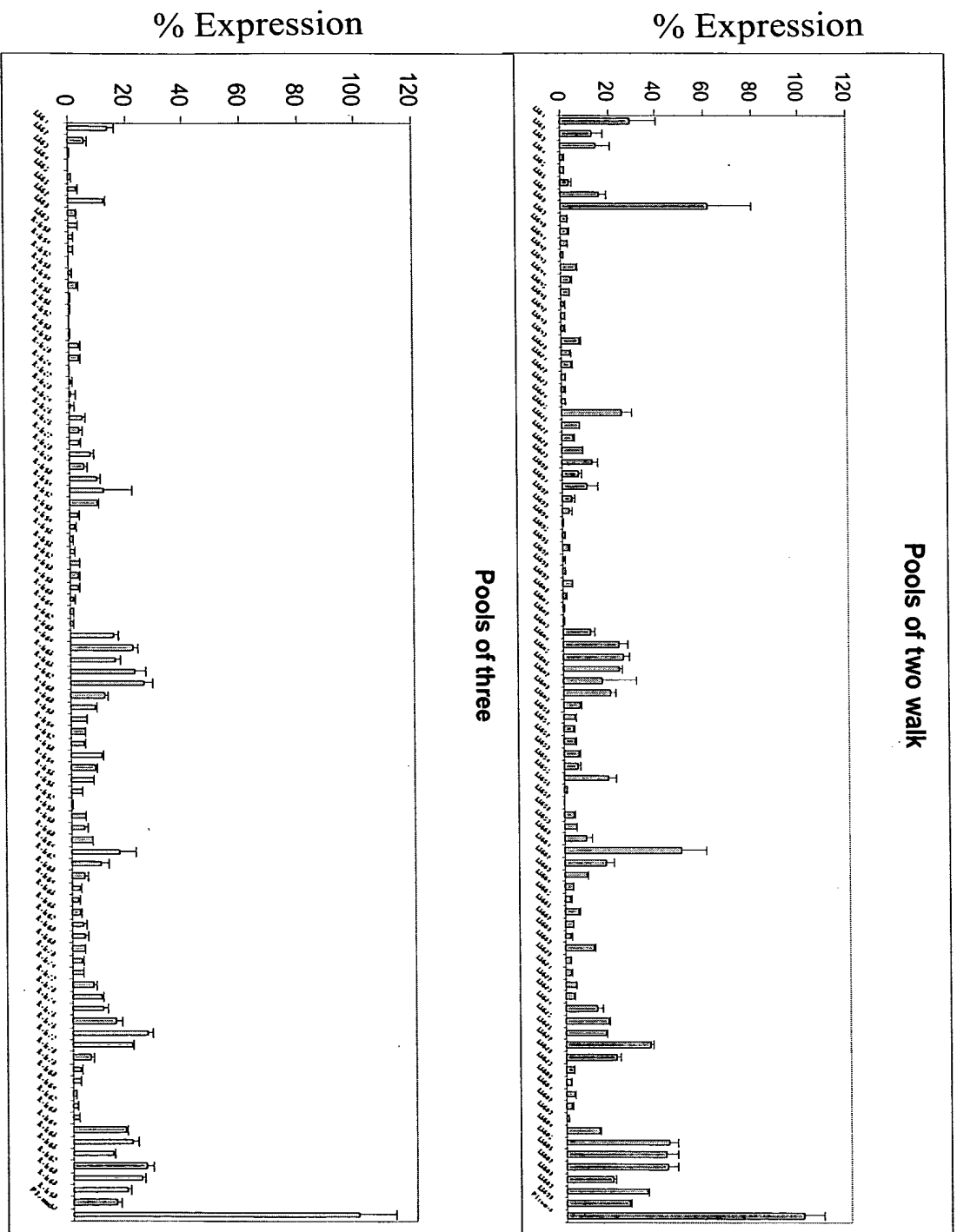


Figure 16

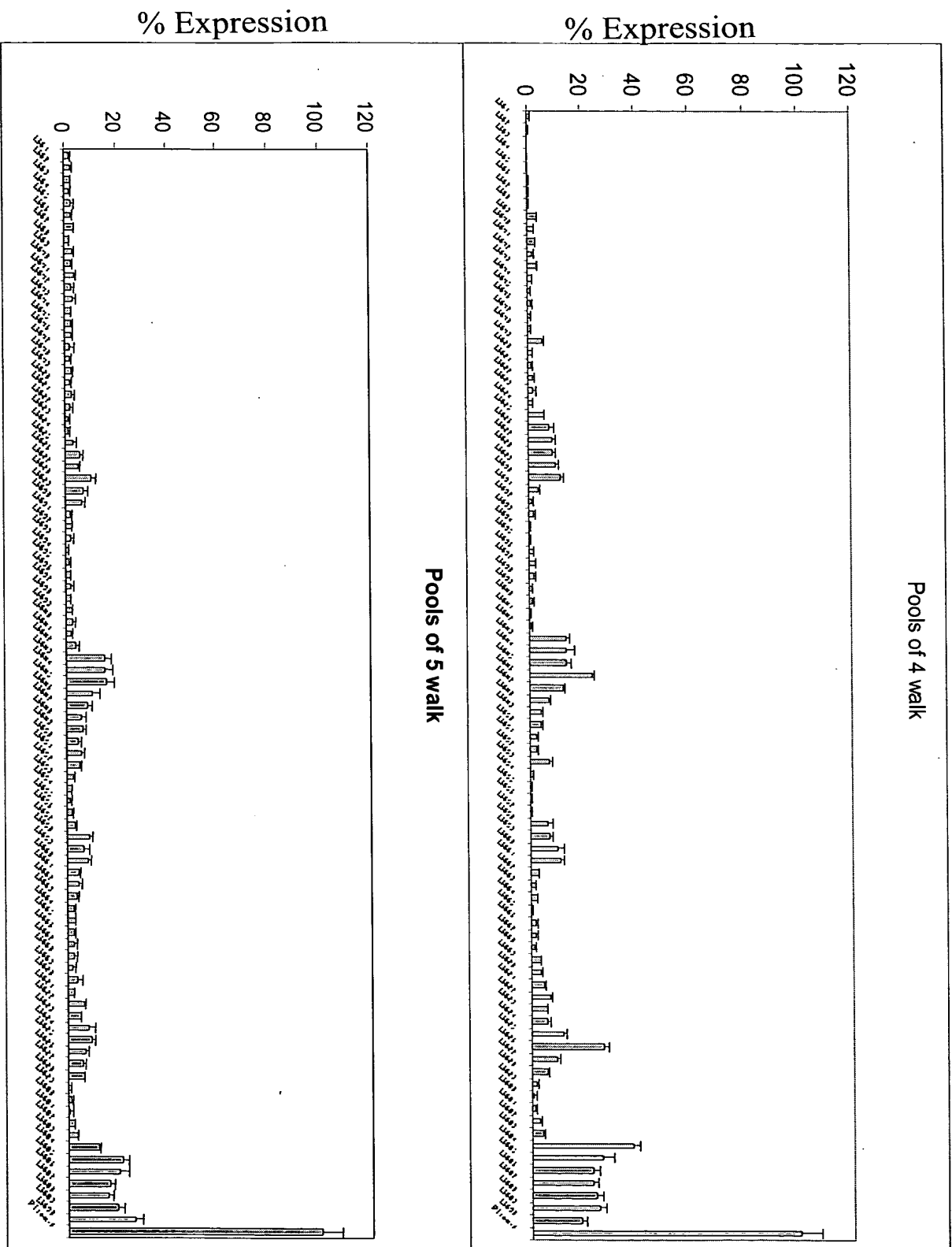


Figure 17

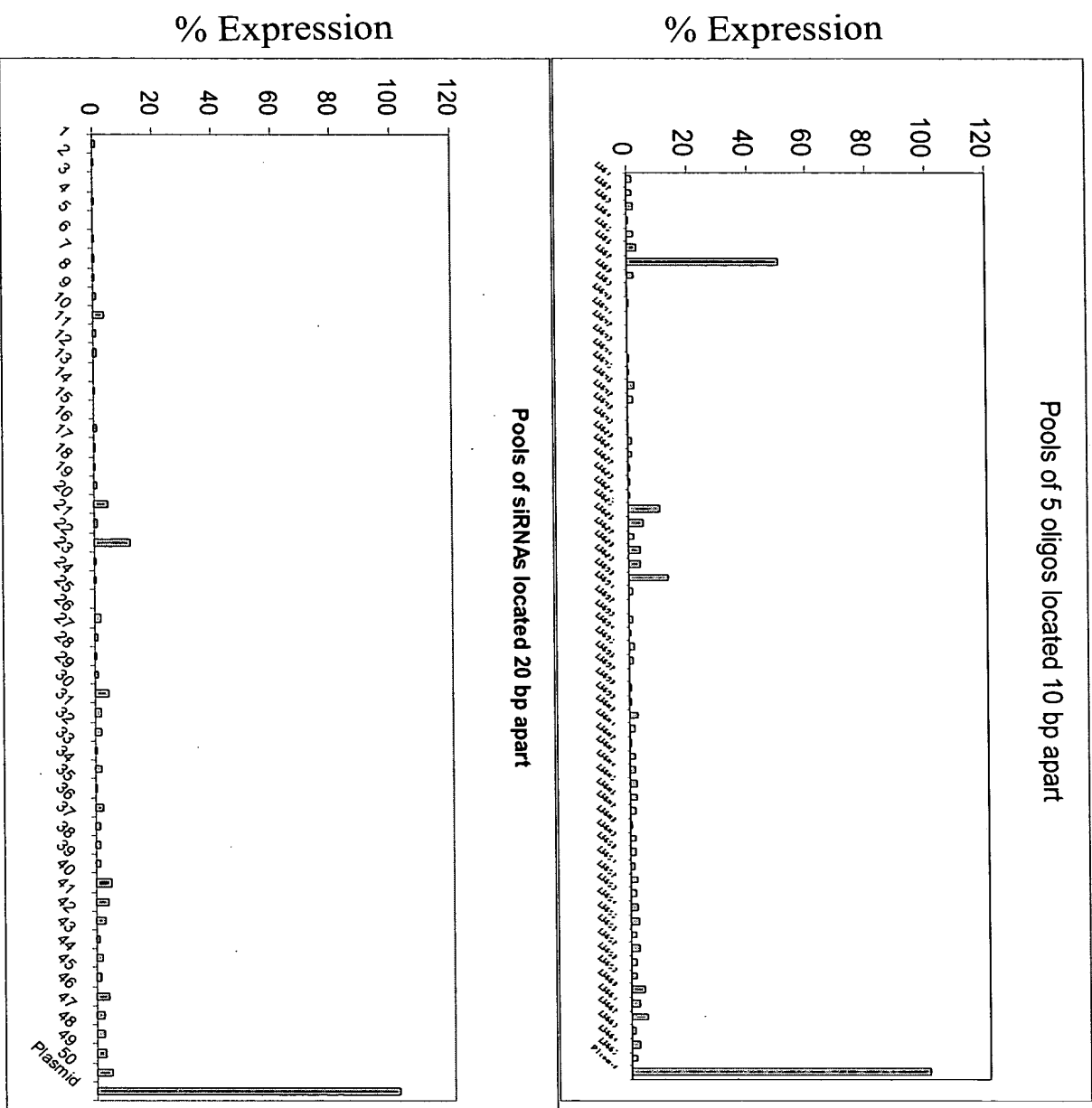


Figure 18



**Combination of several semifunctional siRNAs result in a significant improvement of gene expression inhibition**

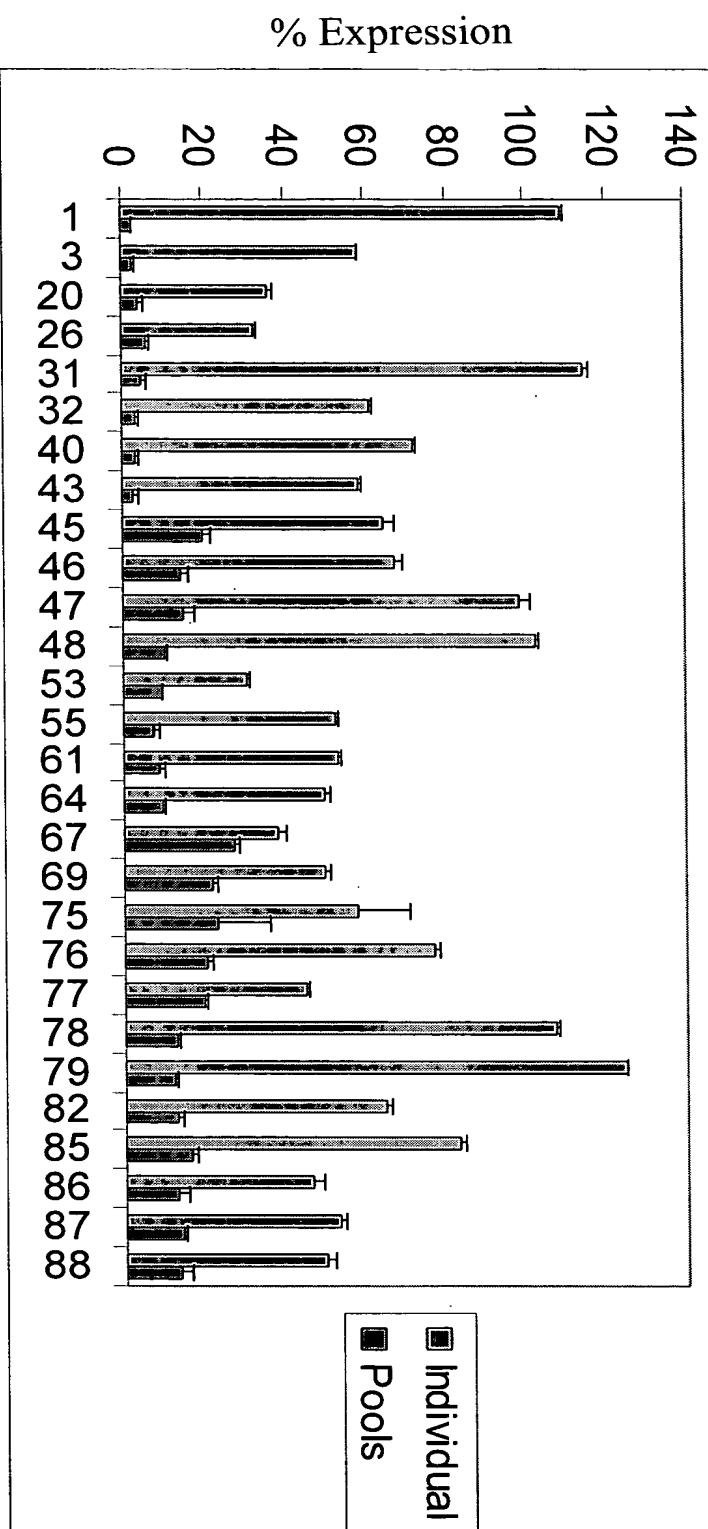


Figure 20

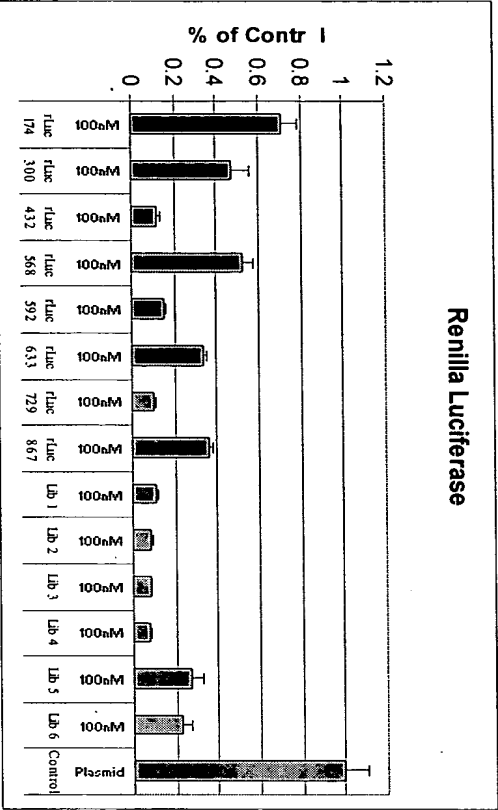
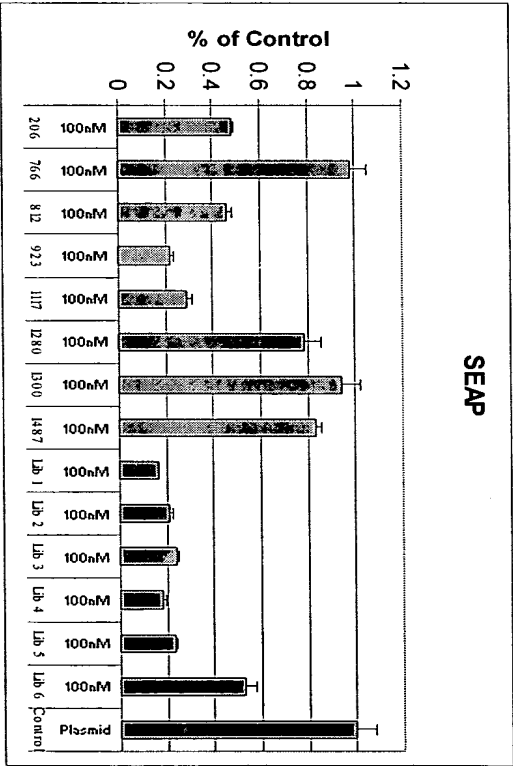
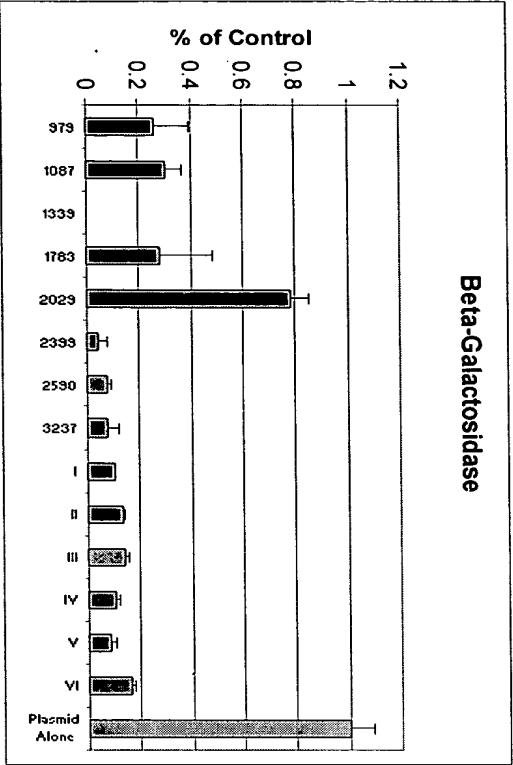


Figure 21



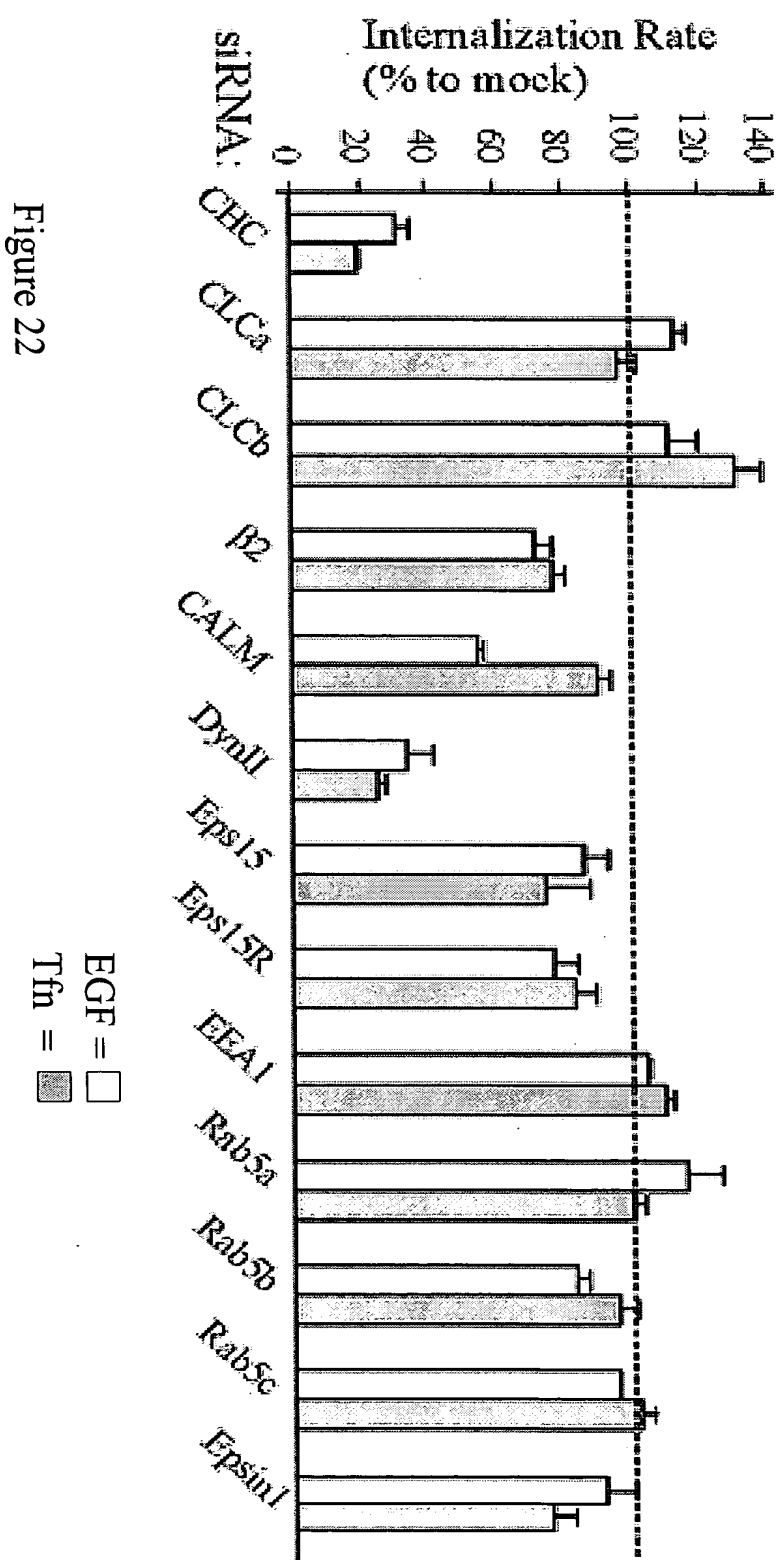


Figure 22

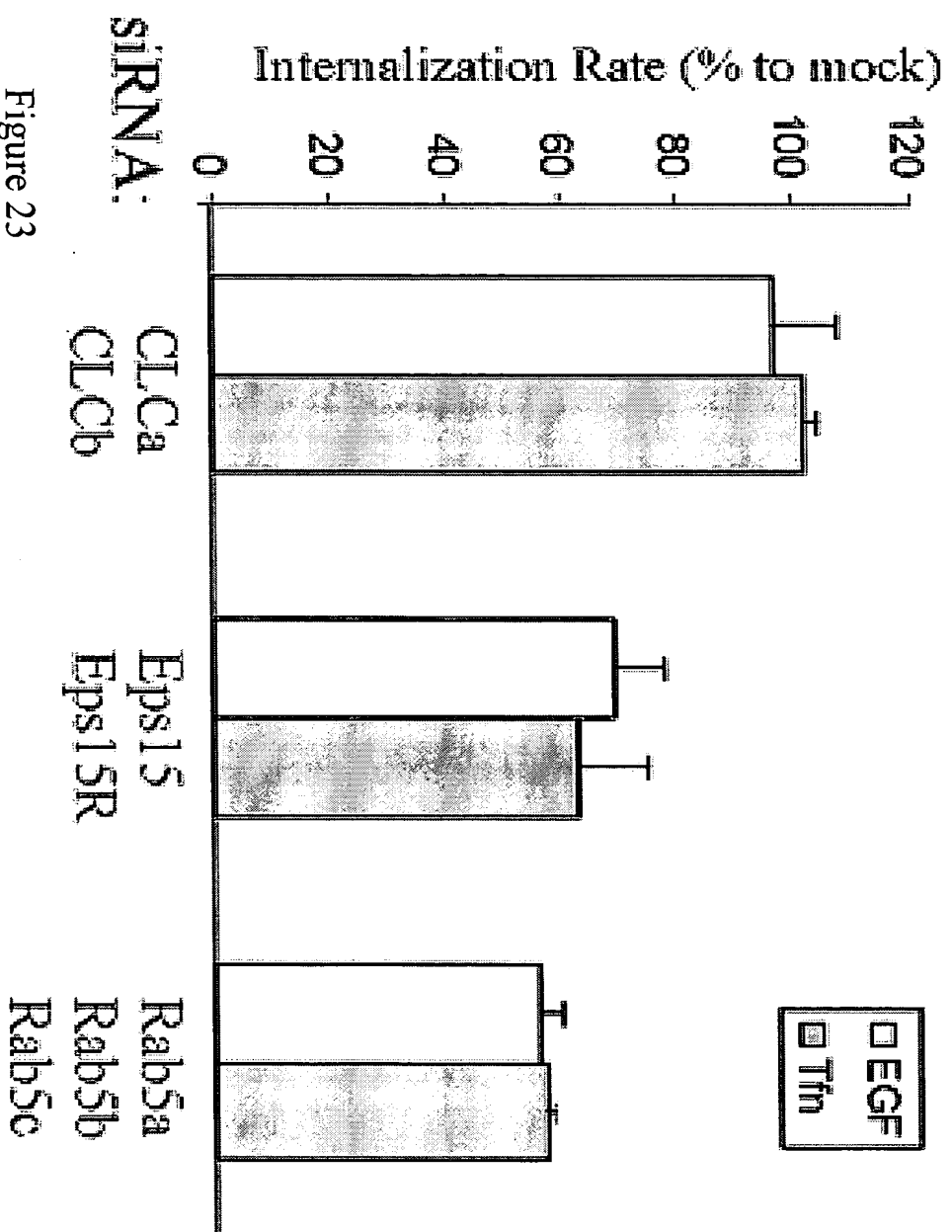


Figure 23

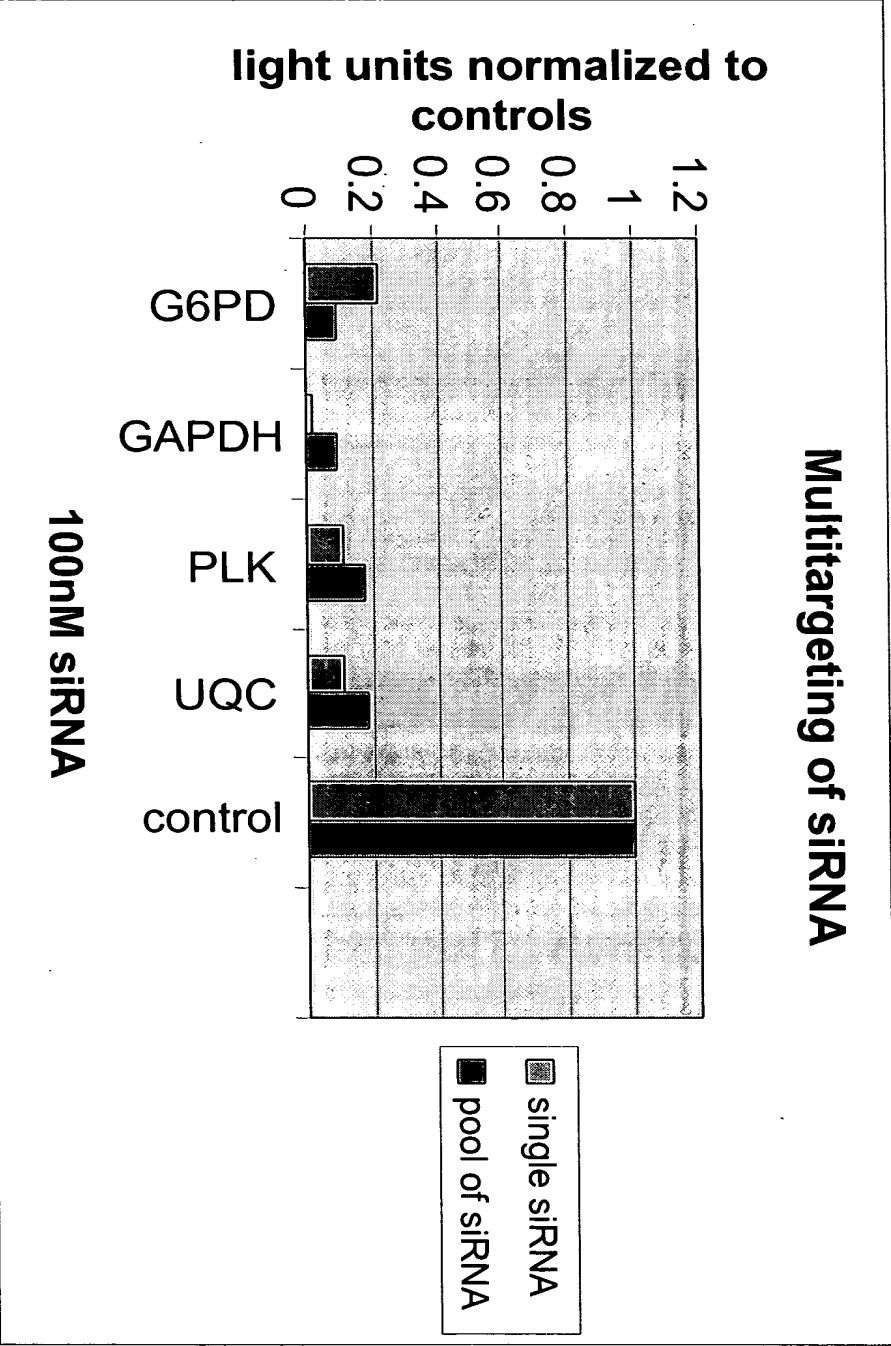


Figure 24

Figure 25

**Bcl-2 knockdown by 10 rationally designed siRNAs at  
300 pM concentration**

